

#### REMARKS

Claims 20-25, 28-32, 35-38 and 41-46 are now pending in this application. Applicants have amended the claims to overcome the Examiner's objections and rejections as described in more detail below. The request for cancellation of claims herein is made without prejudice and applicants preserve their right to obtain claims to the canceled subject matter in divisional or continuing applications claiming priority from this application.

#### RESPONSE TO EXAMINER'S OBJECTIONS

Claim 49 stands objected to because in line 2 "CF<sub>2</sub>F" should read "CH<sub>2</sub>F". Applicants have canceled claim 49 herein, thereby obviating this rejection.

#### RESPONSE TO EXAMINER'S REJECTIONS

##### 35 U.S.C. § 112, first paragraph

Claims 43-48 stand rejected under 35 U.S.C. § 112, first paragraph because the Examiner contends they contain subject matter which was not described in the specification in such a way as to enable one of skill in the art to use the invention. Specifically, the Examiner contends that the specification, while enabling the treatment of autoimmune disease, does not provide enablement for the prevention of autoimmune disease. In order to expedite allowance of the

pending claims, applicants have amended claim 43 (and therefore claims 44-46 which depend therefrom) to delete reference to the prevention of autoimmune disease. Claims 47 and 48 have been canceled. Applicants, therefore, respectfully request that the Examiner reconsider and withdraw the rejection under 35 U.S.C. § 112, first paragraph.

35 U.S.C. § 112, second paragraph

Claims 28 and 43 stand rejected under 35 U.S.C. § 112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention.

Specifically, the Examiner contends that in claim 28 the substituent "Z" is defined but there is no "Z" in the claimed formula. Applicants have amended the formula in claim 28 to delete the substituent "A" and substitute therefor the substituent "Z" thus obviating the rejection. Support for this amendment can be found throughout the specification as originally filed, particularly at page 9, lines 20-28.

The Examiner also contends that the phrase "autoimmune disease" in claim 43 is vague and one of ordinary skill in the art would not be able to ascertain its metes and bounds. Applicants traverse.

One of ordinary skill in the art understands the meaning of "autoimmune disease." Autoimmune disease is defined in the art as a disease "caused by antibodies produced against substances naturally present in the body." (The Oxford Dictionary and Thesaurus American Edition (1996)).\* As such, it is well within the skill of the art to ascertain the metes and bounds of claim 43.

Applicants request that the Examiner reconsider and withdraw the 35 U.S.C. § 112, second paragraph rejections.

#### Double Patenting

##### i. Statutory Type Double Patenting

Claims 20-25 and 28-32 stand rejected under 35 U.S.C. § 101 because the Examiner contends they claim the same invention as claims 1-11 of United States Patent No. 5,756,465.

Claims 1-11 of United States Patent No. 5,756,465 recite compounds and pharmaceutical compositions "comprising an amino acid sequence having an N-terminal blocking group and a C-terminal Asp residue connected to an electronegative leaving group, wherein said amino acid sequence corresponds

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\* For the convenience of the Examiner, applicants have attached a copy of the relevant page from this reference at tab B.

to the sequence Ala-Tyr-Val-His-Asp, residues 112 to 116 of Seq. I.D. No. 3."

However, claims 20-25 and 28-32 of the instant application recite compounds and pharmaceutical compositions "comprising an amino acid sequence having an N-terminal blocking group and a C-terminal Asp residue connected to an electronegative leaving group, wherein said amino acid sequence substantially corresponds to at least a portion of the sequence Ala-Tyr-Val-His-Asp, residues 112 to 116 of Seq. I.D. No. 3." (Claim 20 is used as an example; emphasis is added.)

The claims of the instant invention are thus not coextensive with the claims of United States Patent No. 5,756,465. Applicants therefore respectfully request that the Examiner reconsider and withdraw the double patenting rejections under 35 U.S.C. § 101.

ii. Non-Statutory Double Patenting

Claims 20-27, 28-34 and 49 stand rejected under the judicially created doctrine of double patenting in view of claims 1-11 of United States Patent No. 5,756,465. In order to overcome this rejection, applicants will file a Terminal Disclaimer in compliance with 37 C.F.R. 1.321 upon notice that the claims are otherwise in condition for Allowance.

35 U.S.C. § 102(b)

Claims 20-49 stand rejected under 35 U.S.C. 102(b) as being anticipated by various references. Specifically, the Examiner contends that WO 9305071 ('071, published March 18, 1993), WO 9115577 ('577, published October 17, 1991), Thornberry et al. ("Thornberry", published April 30, 1992) and Rosenthal et al. ("Rosenthal", published November, 1991) were "patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States." Applicants traverse.

These documents were not published before applicants' earliest priority date. The instant application is a continuation of, and claims priority to, United States Application No. 09/039,657 (now issued United States Patent No. 6,136,787) which is a divisional application of United States Application No. 440,179 (now issued United States Patent No. 5,756,465). As such, the instant application is entitled to claim priority from United States Application No. 203,176 (filed February 28, 1994 and now issued United States Patent No. 5,416,013), and United States Application No. 750,644 (filed August 30, 1991).

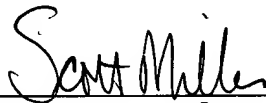
It is clear that the priority date for the instant application of August 30, 1991 is prior to the publication dates of '071, '577, Thornberry and Rosenthal. These documents are, therefore, not prior art to this application.

Applicants therefore request that the Examiner reconsider and withdraw the 35 U.S.C. 102(b) rejections based on these references.

#### CONCLUSION

In view of the foregoing remarks and amendments, applicants request that the Examiner favorably reconsider this application and allow the amended claims now pending in it.

Respectfully submitted,



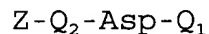
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24, 2002  
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## Appendix A

21. (Amended) The compound according to claim 20 having the formula:



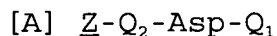
where Z is an N-terminal protecting group;

$Q_2$  is 0 to 4 amino acids such that the sequence  $Q_2$ -Asp substantially corresponds to at least a portion of the sequence Ala-Tyr-Val-His-Asp, residues 112 to 116 of Seq.

I.D. No. 3;

and  $Q_1$  is an electronegative leaving group.[:]

28. (Amended) A pharmaceutical composition comprising a physiologically acceptable carrier and a compound of the formula:



where Z is an N-terminal protecting group;

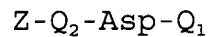
$Q_2$  is 0 to 4 amino acids such that  $Q_2$ -Asp substantially corresponds to at least a portion of the sequence Ala-Tyr-Val-His-Asp, residues 112 to 116 of Seq. I.D. No. 3;

and

$Q_1$  is an electronegative leaving group.[:]

43. (Amended) A method of treating inflammation or [preventing and] treating an autoimmune disease in a

mammal in need of such treatment comprising administering to said mammal an effective amount of a compound of the formula:



where Z is an N-terminal protecting group;

$Q_2$  is 0 to 4 amino acids such that the sequence  $Q_2$ -Asp substantially corresponds to at least a portion of the sequence Ala-Tyr-Val-His-Asp, residues 112 to 116 of Seq. I.D. No. 3; and

$Q_1$  is an electronegative leaving group.[:]



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## autodidact | aut xidation

execution of such a sentence, esp. the burning of a heretic.  
[Port., = act of the faith]

**autodidact** /'ɔ:tədɪ'dækt, -dækt/ *n.* a self-taught person.  
**autodidactic** /-dæktɪk/ *adj.* [AUTO- + *didact* as DIDACTIC]

**autoerotism** /áwtō-erótizəm/ *n.* (also **autoeroticism** /-irōtízizəm/) *Psychol.* sexual excitement generated by stimulating one's own body; masturbation. □ **autoerotic** /-irōtík/ *adj.*

**autofocus** /'aʊtəfəʊkəs/ *n.* a device for focusing a camera, etc., automatically.

**autogamy** /awtógámee/ *n.* Bot. self-fertilization in plants.  
 □ **autogamous** *adj.* [AUTO- + Gk. -gamia *f.* gamos marriage]

**autogenous** /awtəjɪnəs/ *adj.* self-produced. **autogenous welding** a process of joining metal by melting the edges together without adding material.

**autogiro** /áwtōjīrō/ *n.* (also **autogyro**) (*pl.* -os) an early form of helicopter with freely rotating horizontal vanes and a propeller. [Sp. (as **AUTO-**, *giro* gyration)]

**autograft** /'ɔ:təgrɑ:ft/ *n.* Surgery a graft of tissue from one point to another of the same person's body.

**autograph** /'awtəgrəf/ **n.** & **v.** **n.** 1 a signature, esp. that of a celebrity. 2 a handwriting. 3 a manuscript in an author's own handwriting. **3** a document signed by its author. **v.** **n.** 1 sign (a photograph, autograph album, etc.). 2 write (a letter, etc.) by hand. [*F. autographe* or *LL. autographum* f. *G. autographon* neut. of *autographos* (as *AUTO-*, *-GRAPH*)]

**autograph** /aw'tagraf/ *n.* 1 writing done with one's own hand. 2 a photograph of a person's signature. *v.* 1 to sign one's name on a document. 2 to take a photograph of a person's signature.

hand. 2 the facsimile reproduction of writing or illustration  
 ☐☐ autographic /-təgrəfɪk/ *adj.*

**Autoharp** /awtōharp/ *n. propr.* a kind of zither with a mechanism that allows the playing of chords.

**autoimmune** /ˈɔːtəɪmjuːn/ *adj.* *Med.* (of a disease) caused by antibodies produced against substances naturally present in the body. **autoimmunity** *n.*

**autointoxication** /ˌɔːtɒɪntɒksɪkəˈʃən/ *n.* *Med.* poisoning by a toxin formed within the body itself.

**autolysis** /awtólisis/ *n.* the destruction of cells by their own enzymes. **autolytic** /awtólitik/ *adj.* [G *Autolyse* (AUTO-; -LYSIS)]

**Automat** /aw'tomat/ *n. propr.*: a cafeteria containing coin-operated machines dispensing food and drink. [G f. F *automate*, formed as AUTOMATION]

**automate** /awtə'mayz/ v.tr. convert to or operate by automation (the ticket office has been automated). **o** **automatic teller machine** electronic machine that allows customers to insert a card, punch in an identification number, and then perform banking transactions such as depositing or withdrawing funds, etc. **Abbrev.** ATM. [back-form. f. AUTOMATION]

■ automatize. □ automated teller machine *colloq.* cash machine, automatic teller machine.

**automatic** /awtamatik/ *adj.* & *n.* • *adj.* 1 (of a machine, device, etc., or its function) working by itself, without direct human intervention. 2 • done spontaneously, without conscious thought or intention (*an automatic reaction*). 3 • necessary and inevitable (*an automatic penalty*). 3 *Psychol.* 4 • formed unconsciously or subconsciously. 4 (of a firearm) that continues firing until the ammunition is exhausted or the pressure on the trigger is released. 5 (of a motor vehicle or its transmission) using gears that change automatically according to speed and acceleration. • *n.* 1 an automatic device, esp. a gun or transmission. 2 *colloq.* a vehicle with automatic transmission. ◦ *automatic pilot* a device keeping an aircraft on a set course. ◦ *automatically* ◦ *automaticity* /awtəmatistee/ *n.* [formed as AUTOMATO-  
-ic]

■ **adj.** 1 self-acting, self-governing, self-regulating, self-executing, mechanical, robotic; automated. 2 a mechanical, involuntary, instinctive, instinctual, natural, spontaneous, impulsive, immediate, conditioned; unconscious, subconscious; intuitive, reflex, knee-jerk, gut, robotlike, robotic, unbidden. b unavoidable, inevitable, inescapable, ineluctable;

mandatory, compulsory, assured; definite. 3 see sense 2a above. • n. 1 (*spec.*) Mil. machine-gun, MG, Tommy gun, pom-pom, Bren; Gatling (gun), Lewis gun, Sten gun; sl. chopper. o automatic pilot: autopilot, *Brit. sl.* George. o automatically: mechanically, by itself or oneself, on its or one's own; involuntarily, instinctively, instinctually, intuitively, spontaneously, impulsively, immediately, unconsciously, unthinkingly; see also NECESSARILY.

**Automation** /awtómáyshan/ *n.* **1** the use of automatic equipment to save mental and manual labor. **2** the automatic control of the manufacture of a product through its successive stages. [irreg. f. AUTOMATIC + -ATION]

**automatism** /awtómotizəm/ *n.* **1** *Psychol.* the performance of actions unconsciously or subconsciously; such action. **2** involuntary action. **3** unthinking routine. [F *automatisme* f. *automate* AUTOMATON]

**automatize** /awtómáiz/ v.tr. **1** make (a process, etc.) automatic. **2** subject (a business, enterprise, etc.) to automation  
□ **automatization** n. [AUTOMATIC + -IZE]

**automaton** /aw'tə-mən, -tən/ *n.* (pl. *automata* /-tə/ or *automatons*) 1 a piece of mechanism with concealed motive power. 2 a person who behaves mechanically, like an automaton. [L f. Gk, neut. of *automatos* acting of itself: see **AUTO-**]

■ 1 see ROBOT 1, 2. 2 see ROBOT 3.  
**automobile** /*awtəmobeel*/ *n.* a motor vehicle for road use with an enclosed passenger compartment; a car. [F (a AUTO-, MOBILE)]

**automotive** /awtə'mōtɪv/ *adj.* concerned with motor vehicle  
**autonomic** /awtə'nōmɪk/ *adj.* esp. *Physiol.* functioning involuntarily. **an autonomic nervous system** the part of the nervous system responsible for control of the bodily functions not consciously directed, e.g., heartbeat. [AUTONOMY + -ic]  
**autonomous** /awtə'nōməs/ *adj.* 1 having self-government, acting independently or having the freedom to do so. **an autonomous state**  
**autonomously** *adv.* [Gk *autonomos* (as AUTONOMY)]

**autonomy** /awtónómee/ *n.* (pl. -ies) 1 the right of self-government. 2 personal freedom, 3 freedom of the will. 4 a self-governing community. ⇨ **autonomist** *n.* [Gk *autonomia* autos self + *nomos* law]

■ 1 see SELF-GOVERNMENT 1. 2 see FREEDOM 1, 2.  
3 freedom, independence, self-determination.

**autopilot** /ˈɔːtəpɪlət/ *n.* an automatic pilot. [abbr.]  
**autopsy** /ˈɔːtəpsi/ *n.* (pl. -ies) 1 a postmortem examination to determine cause of death, etc. 2 any critical analysis. personal inspection. [F *autopsie* or mod.L. *autopsia* f. Gr. *autopsiēs* eyewitness]

■ 1 postmortem, necropsy. 2 colloq. postmortem; see also ANALYSIS 1.

**autoradiograph** /áwtōráydecəgráf/ *n.* a photograph of object, produced by radiation from radioactive material on the object. **no autoradiographic** *adj.* autoradiographic /áwtōráydiəgráf/ *n.*

**autosuggestion** /ˈɔːtəʊsəʒjəsən/ *n.* a hypnotic or subconscious suggestion made by a person to himself or herself affecting behavior.

**autotelic** /'ɔ:tətɛlɪk/ *adj.* having or being a purpose in itself  
[AUTO- + Gk *telos* end]

**autotomy**/awtótómee/*n.* Zool. the casting off of a part of body when threatened, e.g., the tail of a lizard.

**autotoxin** /*awtōtōksin*/ *n*: a poisonous substance origina-  
 within an organism. **||** **autotoxic** *adj*.

**autotrophic** /awtətrɒfɪk, -trɒ-/ *adj.* *Biol.* able to form complex nutritional organic substances from simple inorganic substances such as carbon dioxide (cf. **HETEROTROPHIC**) [**AUTO-** + Gk *trophos* feeder]

**autotype** /aw'tatip/ *n.* 1 a facsimile. 2 a photographic printing process for monochrome reproduction. 3 a print made by this process.

**autoxidation** /awtóksideyshən/ *n.* Chem. oxidation by exposure to air at room temperature.

and fruits are gathered from September through March to May from the autumn to maturity or in the genus *Colca* and unrelated [autumn 1111] 11/11.

**auxiliary** /awtūn  
 relate to autumn  
**auxiliary** /awtūn  
 past the prime of  
**auxiliary** /awgzil  
 thing) that gives  
 thing additional.  
 thing. 3 (in pl.)  
 with o auxiliary  
 but different nation  
 in firming tenses  
 phrase f. *auxiliu*  
 o ad. supportive  
 supplementar  
 secondary, ex  
 support, accep  
 bipennate, ma  
 deputy.

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 2. audio  
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 8. evil (v.)  
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to attend

posterior (av-  
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a carry down  
other order d  
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tower, esp. l  
progressive.  
[guard])

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- garment)
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equality.  
in Malware  
inexpensive  
page 111